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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/664,234	RUAN ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2008*.

2a)☒ This action is FINAL. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29 and 31-54* is/are pending in the application.

4a) Of the above claim(s) *1-24,42 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-29,31-41,44-49 and 53* is/are rejected.

7)☒ Claim(s) *40,41,50-52 and 54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0708*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is responsive to the Response including a complying complete set of claims filed October 31, 2008. Claims 25-29, 32-37, 39-41, 44, 47-48, and 51 have been amended and claim 30 has been canceled. Claims 1-24 and 42-43 remain withdrawn (see below). Claims 25-29, 31-41 and 44-54 are now pending and under consideration. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow and/or are moot in view of the new grounds of rejection set forth below. Any rejections and/or objections not reiterated in this action have been withdrawn. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

3. Claims 1-24 and 42-43 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on December 9, 2005. In light of the species election requirement applied to claim 35 (see the restriction requirement of October 11, 2005), and applicant's election of MmeI (see the reply of December 9, 2005), restriction enzymes other than MmeI are also withdrawn from further consideration. Election was made without traverse in the reply filed on December 9, 2005.

Information Disclosure Statement

4. The information disclosure statement filed July 7, 2008 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the citations for cite numbers 17 and 18 are not complete. Specifically, no date has been provided for the cited material, and it is noted that the date on the material itself is truncated, such that the examiner was unable to complete these citations. Accordingly, these citations have been crossed through on the IDS. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Claim Objections

5. Claims 40-41 are objected to because of the following informalities: claim 40 recites "the 3'-terminus sequence cDNA transcript" rather than "the 3'-terminus sequence of a cDNA transcript". As this appears to be a typographical error, the claim is interpreted as reciting "the 5'-terminus sequence and the 3'-terminus sequence of a cDNA transcript". However, appropriate correction is required.

6. A typographical error in claim 44 ("cDNa") is noted.

7. Claims 50-52 and 54 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Specification

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 18). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112, second paragraph

9. Claims 28, 39 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANT'S AMENDMENTS:

Claim 28 has been amended to state that "the concatemer of ditags are 1-1000 ditags." To the extent that the "concatemer" consists of a single ditag, it is unclear how, or even whether, this claim further limits the claims from which it depends. It is noted that a proper dependent claim must further limit the claims from which it depends, and that a "concatemer" having a single ditag does not appear to meet this requirement. It is unclear what is meant by the language of claim 28, as claim 27 (from which claim 28 depends) clearly requires a "concatemer of ditags". Accordingly, clarification is required with respect to claim 28. It is noted that the linking of a ditag to 1 to 1000 other ditags (as taught at, e.g., page 7, lines 4-5 of the specification) would require at least 2 ditags.

Claim 39 is indefinite over the recitation of the phrase "defining the corresponding gene on the genome map." Neither the specification nor the prior art make clear what is

required by the language "defining" a gene on a genome map, and it is therefore unclear what type of action or manipulation (if any) is actually required by this recitation. It is noted that while applicant's reply addresses the prior rejection of claim 39 with respect to the language "structural region", this language has been deleted from the claim, and the term "defining" and its meaning within the context of the invention is not addressed. Accordingly, clarification is required.

Claim 41 is indefinite over the recitation of the language "the full-length cDNA corresponding to the ditag". As the claims do not previously refer to such a molecule, it is unclear what constitutes 'the full-length cDNA corresponding to the ditag." There is insufficient antecedent basis for this terminology.

Claim Rejections - 35 USC § 112, first paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANT'S AMENDMENTS:

11. Claims 48-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 48-49 depend from claims 26 and 29. Claim 26 as amended requires extraction of tags from the 5' and 3' termini of a full-length cDNA flanked by adapters to produce a ditag including the adapters, and claim 29 further requires including this ditag in a vector. Claim 48 then requires that the vector in which the ditag is included comprises "at least a full length cDNA transcript and two adapters flanking" the transcript; thus, the vector of claims 48-49 requires both a ditag flanked by adapters and a full length cDNA flanked by adapters. While the specification does disclose vectors including ditags flanked by adaptors (as set forth in claim 29), as well as vectors comprising full length cDNAs (see, e.g., pages 19-23 of the specification), the particular constructs now embraced by the amended version of claims 48-49 is not disclosed. Accordingly, applicant's amendments of October 31, 2008 have introduced new matter into claims 48-49.

Claim interpretation

12. It is again noted that the specification does not provide a limiting definition for the term "ditag." At page 4, the specification refers to "two tags (a ditag) per nucleic acid molecule," such that this language broadly encompasses any two "tag" sequences that may be obtained from a single nucleic acid molecule. It is also noted that, as previously discussed on the record in the reply of August 28, 2006 and the Office action of January 7, 2008, the terms "3' terminus" and "5' terminus" as employed in the claims refer to a terminal region or portion (as opposed to a single, terminal nucleotide).

Claim Rejections - 35 USC § 102

13. In view of the cancellation of claim 30, the prior rejection of that claim under 35 USC 102(b) is moot.

14. In view of the amendment of claim 25 to require a "full length cDNA transcript" and the amendment of claim 39 to require a "cDNA transcript corresponding to the full-length of a gene," the prior rejection of claims 25 and 39 under 35 U.S.C. 102(b) as being anticipated by Macevicz (US 6,054,276 A [25 April 2000]; hereinafter referred to as Macevicz-II) is withdrawn.

15. The following are new grounds of rejection necessitated by applicant's amendments. Although the claims were previously rejected as being anticipated by the same reference, applicant's amendments have necessitated the inclusion of new grounds in the present rejection. It is noted that, to the extent that they apply to the present rejection, applicant's arguments are addressed following the rejection.

16. Claims 25-29, 31, 33-35, 37-38, 44-49, and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Macevicz (US 6,136,537 [issued 24 October 2000]).

Macevicz discloses a modification of the serial analysis of gene expression (SAGE) method in which pairs of sequence tags are constructed using a portion of each end of a target polynucleotide such as a cDNA (see entire reference, particularly the summary at col 2, line 17-col 3, line 19). With regard to applicant's claims as presently amended, Macevicz teaches that cDNAs are preferred for use in his methods (see, e.g., col 4, lines 25-26), and explicitly teaches the use of full length cDNAs in his methods

(see, e.g., col 8, line 56-col 9, line 3). Macevicz discloses, e.g., a method in which the nucleic acid molecule of interest is inserted into a vector, and subsequently cleaved, linearized, and recircularized to form a tag pair or "ditag" including the 5' and 3' terminus of the nucleic acid molecule (see, e.g., col 2, lines 32-67; col 4, line 20-col 10, line 45). It is an inherent property of each such tag that it has a 5' and 3' end, and Macevicz further teaches that recircularization to form ditags is achieved by ligation (see col 7, lines 9-11), which inherently constitutes the joining/ligation of the 3' end of the 5' tag to the 5' end of the 3' tag. Macevicz further discloses producing the nucleic acid molecules employed in his methods (see, e.g., col 4, lines 20-65; col 8, line 21-col 9, line 3); Macevicz therefore discloses all 3 steps of claim 25, and anticipates that claim.

Regarding claim 26 and claims dependent therefrom, Macevicz also discloses the production and use in his method of nucleic acid molecules flanked by linkers so as to produce ditags flanked by linkers (see, e.g., col 4, lines 20-65, particularly lines 50-52; col 6, lines 26-52); it is a property of such linkers that they constitute a type of adaptor. Macevicz also explicitly discloses the ligation of adaptors to the ends of nucleic acid molecules at, e.g., col 10, lines 19-45. Accordingly, Macevicz anticipates claim 26. Regarding claims 27-28, Macevicz discloses a step of creating concatemers of ditags (see, e.g., col 2, lines 64-67; col 9, lines 46-55). Regarding claim 28, Macevicz teaches concatemers of several hundred base pairs, and therefore discloses quantities of ditags meeting the requirements of claim 28 in a single concatemer molecule. With respect to claim 31, Macevicz discloses sequencing of ditags to determine gene expression (see, e.g., col 9,lines 52-55). Regarding claims 33-35 and 37, it is again

noted that Macevicz discloses the addition of linkers/adaptors (see, e.g., col 4, lines 20-65, particularly lines 50-52; col 6, lines 26-52; col 10, lines 19-45), and that Macevicz further discloses the use of multiple adaptors comprising multiple asymmetric recognition sites, and specifically discloses the elected MmeI restriction site (see, e.g., col 10, lines 10-45; col 7, lines 28-50, particularly line 52; see also col 4, line 37). With further regard to claim 37, Macevicz specifically disclose the use of such adaptors with cDNA at, e.g., col 10, lines 41-45. Regarding claim 38, Macevicz discloses ditags comprising 34-38 nucleotides; see, e.g., col 9, line 64.

Regarding claim 29 and claims dependent therefrom, it is again noted that Macevicz teaches construction of his ditags in a vector (see again col 2, lines 17-67; see also col 6, line 26-col 7, line 27). Regarding claims 44-49 and 53, vectors and adaptors meeting the requirements of the claims are disclosed at, e.g., col 10, lines 10-45, and the disclosure of MmeI is again noted (see col 4, line 37 and col 7, line 52). With further regard to claims 46-49, it is also noted that Macevicz teaches selection of a vector "which does not contain a recognition site...for the type IIs enzyme(s) used to generate pairs of segments; otherwise, re-circularization cannot be carried out" (see col 7, lines 43-47).

Regarding applicant's arguments pertaining to the prior rejection of the claims as being anticipated by Macevicz, it is noted that Macevicz does in fact teach the use of full length cDNAs in his methods, as discussed above. Regarding the teachings of Macevicz at col 6, lines 22-23, it is noted that this portion of Macevicz pertains to an embodiment of Macevicz's invention in which restriction enzymes are not employed;

however, Macevicz in fact teaches the use of restriction enzymes, including the preferred MmeI enzyme elected by applicants, as noted above. In fact, this portion of Macevicz would suggest to one of ordinary skill that the embodiments of Macevicz's inventions involving the use of restriction enzymes would be preferred with full length cDNAs. Further, applicant's claims clearly embrace the use of restriction enzymes. Thus, applicant's arguments are not persuasive.

Claim Rejections - 35 USC § 103

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. The following are new grounds of rejection necessitated by applicant's amendments. Although the claims were previously rejected as being obvious over some of the same combinations of references, applicant's amendments have necessitated the inclusion of new grounds in the present rejections. It is noted that, to the extent that they apply to the present rejections, applicant's arguments are addressed following the rejections.

19. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Macevicz (US 6,136,537 [issued 24 October 2000]) in view of Saha et al (Nature Biotechnology 19:508-512 [5/2002]).

Macevicz discloses a modification of the serial analysis of gene expression (SAGE) method in which pairs of sequence tags are constructed using a portion of each end of a target polynucleotide such as a cDNA (see entire reference, particularly the summary at col 2, line 17-col 3, line 19). With regard to applicant's claims as presently amended, Macevicz teaches that cDNAs are preferred for use in his methods (see, e.g., col 4, lines 25-26), and explicitly teaches the use of full length cDNAs in his methods (see, e.g., col 8, line 56-col 9, line 3). Macevicz discloses, e.g., a method in which the nucleic acid molecule of interest is inserted into a vector, and subsequently cleaved, linearized, and recircularized to form a tag pair or "ditag" including the 5' and 3' terminus of the nucleic acid molecule (see, e.g., col 2, lines 32-67; col 4, line 20-col 10, line 45). It is an inherent property of each such tag that it has a 5' and 3' end, and Macevicz further teaches that recircularization to form ditags is achieved by ligation (see col 7, lines 9-11), which inherently constitutes the joining/ligation of the 3' end of the 5' tag to the 5' end of the 3' tag. Macevicz further discloses producing the nucleic acid molecules employed in his methods (see, e.g., col 4, lines 20-65; col 8, line 21-col 9, line 3). Macevicz also discloses the production and use in his method of nucleic acid molecules flanked by linkers so as to produce ditags flanked by linkers (see, e.g., col 4, lines 20-65, particularly lines 50-52; col 6, lines 26-52); it is a property of such linkers

that they constitute a type of adaptor. Macevicz also explicitly discloses the ligation of adaptors to the ends of nucleic acid molecules at, e.g., col 10, lines 19-45.

While Macevicz discloses the sequencing of ditags to determine gene expression (see, e.g., col 9,lines 52-55), Macevicz does not disclose mapping ditag sequences to a database comprising genomic sequences.

Like Macevicz, Saha et al disclose methods in which short sequence tags obtained from gene transcripts are employed in expression analysis (see entire reference). Saha et al disclose querying the human genome sequence database to determine the genes corresponding to tags (see page 509). As the tags of Macevicz comprise the 5' and 3' termini of the nucleic acid molecules being analyzed, the performance of the method of Saha et al using the tags of Macevicz would result in mapping both 5' and 3' termini, as required by the claim.

In view of the teachings of Saha et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Macevicz so as to have performed the further step taught by Saha et al of querying genetic databases to identify genes corresponding to the ditags of Macevicz. Saha et al teach that such further analysis of expression tags is "complementary to other approaches for gene identification," allows "identification of regions not annotated by other methods," and is "an order of magnitude more efficient" than EST sequencing (see page 510, right column). Thus, an ordinary artisan would have been motivated to have made such a modification in order to have achieved any of these advantages specifically taught by Saha et al.

Regarding applicant's arguments pertaining to the prior rejection of the claim as being obvious over the present combination of references, it is again noted that Macevicz does teach the use of full length cDNAs, as discussed above. Further, Saha et al provide general motivation to map expression tags, as noted above, and the present claims recite open transitional language that does not preclude the use of further steps. Additionally, it is noted that claim 32 merely requires mapping "to a database comprising genomic sequences" (i.e., the claim does not in fact require obtaining full length gene sequences). Accordingly, applicant's arguments are not persuasive.

20. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Macevicz (US 6,136,537 [issued 24 October 2000]) in view of Belfort et al (Nucleic Acids Research 25(17):3379-3388 [1997]).

Macevicz discloses a modification of the serial analysis of gene expression (SAGE) method in which pairs of sequence tags are constructed using a portion of each end of a target polynucleotide such as a cDNA (see entire reference, particularly the summary at col 2, line 17-col 3, line 19). With regard to applicant's claims as presently amended, Macevicz teaches that cDNAs are preferred for use in his methods (see, e.g., col 4, lines 25-26), and explicitly teaches the use of full length cDNAs in his methods (see, e.g., col 8, line 56-col 9, line 3). Macevicz discloses, e.g., a method in which the nucleic acid molecule of interest is inserted into a vector, and subsequently cleaved, linearized, and recircularized to form a tag pair or "ditag" including the 5' and 3' terminus of the nucleic acid molecule (see, e.g., col 2, lines 32-67; col 4, line 20-col 10, line 45).

It is an inherent property of each such tag that it has a 5' and 3' end, and Macevicz further teaches that recircularization to form ditags is achieved by ligation (see col 7, lines 9-11), which inherently constitutes the joining/ligation of the 3' end of the 5' tag to the 5' end of the 3' tag. Macevicz further discloses producing the nucleic acid molecules employed in his methods (see, e.g., col 4, lines 20-65; col 8, line 21-col 9, line 3). Macevicz also discloses the production and use in his method of nucleic acid molecules flanked by linkers so as to produce ditags flanked by linkers (see, e.g., col 4, lines 20-65, particularly lines 50-52; col 6, lines 26-52); it is a property of such linkers that they constitute a type of adaptor. Macevicz also explicitly discloses the ligation of adaptors comprising asymmetric restriction sites to the ends of nucleic acid molecules at, e.g., col 10, lines 19-45. However, Macevicz does not disclose the use of an asymmetric restriction site that "is a homing endonuclease asymmetric recognition site sequence" recognized by any of the enzymes set forth in claim 36.

Belfort et al teach that homing endonucleases are rare-cutting enzymes (see entire reference, particularly page 3379 and 3385, right column), and that such enzymes include I-CeuI, PI-SceI, PI-PspI, and I-SceI (see, e.g., Table 2). In view of the teachings of Belfort et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Macevicz so as to have employed adaptors including restriction sites for any of the endonucleases taught by Belfort et al, including any of I-CeuI, PI-SceI, PI-PspI, and I-SceI. It is noted that Macevicz teaches selection of a vector for use in his methods "which does not contain a recognition site...for the type IIs enzyme(s) used to generate

pairs of segments; otherwise, re-circularization cannot be carried out" (see col 7, lines 43-47). Thus, it would have been obvious to an ordinary artisan to have selected for use in adaptors any recognition site for a rare-cutting enzyme (including any of those taught by Belfort et al) for the advantage of employing recognition sites that would be less likely to be present in a vector used in the method of Macevicz.

With regard to applicant's arguments pertaining to the prior rejection of claim 36, those arguments relate to the alleged deficiencies of the Macevicz reference, and therefore have been previously addressed. The Belfort reference was relied upon only for its teachings pertaining to rare cutting enzymes as indicated above.

21. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Macevicz-II in view of Macevicz.

Macevicz-II discloses methods of genomic mapping and gene expression monitoring in which pairs of sequences obtained from each end of a restriction fragment are employed (see entire reference, particularly the summary at col 1, line 60-col 2, line 56). In preferred embodiments, Macevicz-II discloses providing populations of restriction fragments or cDNAs, excising each end thereof, ligating the ends together to form pairs, and employing the pairs or concatenations thereof in mapping, sequence analysis, etc. (see, e.g., col 2, lines 15-56; col 3, line 65-col 4, line 10; claims 5-6). The ligating of ends and concatemerization of pairs taught by Macevicz-II results in the formation of molecules that constitute at least one "ditag" as set forth in applicants' specification, and including "joined" tags as set forth in the claims. Macevicz-II also discloses the use of concatemers of multiple ditags obtained from nucleic acid

populations including cDNAs in mapping (see, e.g., col 2, lines 40-56; col 7, line 64-col 8, line 61), and particularly teaches comparing ditags with a map at, e.g., col 8, lines 20-50. Such mapping inherently results in "defining the corresponding gene on the genome map," as required by the claim (see, e.g., col 2, lines 40-56; col 7, line 64-col 8, line 61). However, while Macevicz-II teaches the use of cDNAs in their methods, Macevicz-II does not teach the use of a cDNA transcript "corresponding to the full-length of a gene," as required by the claim.

Like Macevicz-II, Macevicz teaches a modification of the serial analysis of gene expression (SAGE) method in which pairs of sequence tags are constructed using a portion of each end of a target polynucleotide such as a cDNA (see entire reference, particularly the summary at col 2, line 17-col 3, line 19). With regard to applicant's claims as presently amended, Macevicz teaches that cDNAs are preferred for use in his methods (see, e.g., col 4, lines 25-26), and explicitly teaches the use of full length cDNAs in his methods (see, e.g., col 8, line 56-col 9, line 3). It is a property of such full length cDNAs that they "correspond to" the full length of a gene, and therefore meet the requirements of the claims. Macevicz teaches that "it may be desirable" to employ such full length cDNAs, stating that "In this way, cDNAs that are randomly truncated near their 5' ends are minimized and a source of noise in the gene expression measurements is reduced or eliminated" (col 8, lines 56-61).

In view of the teachings of Macevicz, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Macevicz-II so as to have employed therein full length cDNAs in lieu of or in

addition to the cDNAs taught by Macevicz-II. An ordinary artisan would have been motivated to have made such a modification because Macevicz explicitly teaches that it is desirable to use such full length cDNAs, and/or further for the advantages taught by Macevicz (to minimize the use of randomly truncated molecules and to reduce or eliminate noise).

22. Claims 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macevicz-II in view of Macevicz as applied to claim 39, above, and further in view of Saha et al.

Macevicz-II and Macevicz do not teach the further steps of database comparison and "detecting no match on one or more gene database," as set forth in claim 40, or the further step set forth in claim 41 of "recovering the full-length nucleic acid molecule" corresponding to the ditag.

Like Macevicz-II and Macevicz, Saha et al disclose methods in which short sequence tags obtained from gene transcripts are employed in expression analysis and genome mapping (see entire reference). Saha et al disclose querying the human genome sequence database to determine the genes corresponding to tags (see page 509), and disclose the further analysis of unmatched tags that "represent potential undiscovered genes or unrecognized exons of previously annotated genes" by PCR of DLD-1 cell cDNA followed by further analysis (see page 510). The unmatched tags taught by Saha et al have "no match on one or more gene database," as set forth in claim 40, and the PCR taught by Saha et al constitutes "recovering" a "full-length nucleic acid molecule" corresponding to a newly discovered gene, as required by claim

41. In view of the teachings of Saha et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Macevicz-II in view of Macevicz so as to have performed the further steps taught by Saha et al of querying genetic databases to identify both previously identified and novel genes corresponding to ditags , and to have further analyzed and characterized any unmatched ditags using the steps suggested by Saha et al. Saha et al teach that such further analysis of expression tags is "complementary to other approaches for gene identification," allows "identification of regions not annotated" by other methods," and is "an order of magnitude more efficient" than EST sequencing (see page 510, right column). Thus, an ordinary artisan would have been motivated to have made such a modification in order to have achieved any of these advantages specifically taught by Saha et al.

Double Patenting

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANT'S AMENDMENTS:

24. Claim 25 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 and 24-26 of copending Application No. 11/045,468 (corresponding to published application US 2005/0255501 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 25 is anticipated by the '468 claims. Specifically, independent claim 1 of the '468 application includes steps of preparing a nucleic acid molecule fragment (which constitutes "producing" a nucleic acid molecule as set forth in instant claim 25), cleaving the fragment to extract 5' and 3' tags, and generating a ditag by ligating the tags (see steps (ii) and (iii)). Although the '468 claims do not reference a "full length cDNA transcript" as recited in the instant claims as amended, the specification of the '468 application at page 4, lines 5-7, defines the term nucleic acid molecule fragment as encompassing full length cDNAs. Thus, to the extent that the fragments of the '468 claims are such full length cDNAs, the '468 claims are anticipatory with regard to the instant claims. Alternatively, it would have been obvious to one of ordinary skill in the art to have employed in the claims any of the types of fragments defined as being embraced by the term "fragment" in the present claims. As discussed in MPEP 804, the specification can properly be used as a dictionary to learn the

meaning of a claim term. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

25. With regard to the obviousness-type double patenting rejection over copending application 11/045,468 set forth in the Office action of January 7, 2008, it is noted that applicant again requested in the Response of October 31, 2008 that the rejection be held in abeyance until claims of the instant application have found to be in condition for allowance. Applicant's request is noted. Claim 25 is now rejected for the reasons set forth above.

Conclusion

26. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634